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Study the effect of acidity function on the kinetic of the two complexes formation produced from the reaction of salicylic acid with two diazotized reagents.

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Abstract

The spectrophotometric method was used to the kinetics study of the formation reactions for colored drug complexes derived from electron-donating salicylic acid drug with the two diazotized reagents of (para-nitro aniline) and (sulfanilic acid sodium salt) at the acidic functions (pH4.9, pH7.1 and pH9.3) that accept these electrons at different acidic media The optimal concentration ratios of the two drug complexes with the two reagents were (1:10) for (drug:reagent), respectively. Experimentally , the kinetics of the formation of each drug complex was studied under its optimum conditions and at the three pH levels. It was proved that drug complex formation followed a pseudo first order kinetic with respect to drug. The obtained results were discussed with an appropriate explanation for each one.

Keywords: drug complexes ; kinetic parameters ; pseudo first order kinetic ; diazotized reagent ; Spectrophotometry ; half live tim

Introduction

The attention of many researchers has recently turned to the preparation and study of a type of complex known as (donor - acceptor) complexes using absorption spectra in the visible and ultraviolet regions (UV- Visible spectra) of the spectrum[1-2] because of this type of complexes of great importance, especially in Medical and Biology fields. The ease and accuracy of the spectral method[1] and the availability of its requirements in many laboratories is what encouraged researchers to apply it in determining the stoichiometry of different colored complexes, and then determine the stability constants of these resulting complexes and the factors affecting them by determining the thermodynamic parameters for them at different temperatures As well as kinetic parameters to its activation. The diazonium salts[3-8] prepared from the reaction of amines with nitrous acid by treating sodium nitrite with a solution of amine in hydrochloric acid at (0-5°C) are important compounds in the manufacture of many organic compounds, including the azo imine complexes. As in the following equation: $ArNH_2 + HNO_2 + HX \rightarrow ArN + {}_2X - + 2H_2O$

Salicylic acid[9-14] is a colorless aromatic carboxylic acid that is naturally extracted from some plants such as white willow and meadowsweet. Warts and boils and useful in fighting acne is the main compound of several well-known drugs, especially aspirin. The chemical structure of salicylic acid has

the formula C6H4(OH)COOH, where it is an (OH) group ortho to a carboxyl group. It is also known as 2-hydroxybenzenecarboxylic acid. It is poorly soluble in water (0.2 ml g/100 H_2O at 20°C)[9-14] . In 2005 AD, the researcher Olakunle[15] and his group studied the kinetics of thermal dissociation of the ion (4-Carboxyl-2,6- dinitrobenzene diazonium) (CDNBD) by estimating the small amounts of this ion after each time period by means standard reagent as a sample for repeating two azo groups (diazo). This is in addition to estimating the rate constants for the thermal decomposition process graphically. Another group of researchers[16] has studied the kinetics of the diazotization reactions of benzotriazole as an important organic compound in the main industrial applications. The results confirmed that the kinetic equation for the above reaction is of the first order for each of ortho-phenylene diamine and nitrous acid. The rate constant is a function of temperature. As for our current kinetic study, it includes the kinetics of the formation of the two complexes resulting from the reaction of the electron-donating (salicylic acid drug) with the two diazotized reagents, which are (diazotized sulfanilic acid sodium salt) and (diazotized para-nitro aniline) that accept these electrons, and the determination of the rate of the mentioned reaction , its rate constant(k) , and the half-life time($t_{1/2}$) at the three pH functions (pH4.9, pH7.1 and pH9.3) with an indication of the effect of the pH function on them. What was mentioned above is a small part of what is contained in the literature of this type of studies, and if we limit ourselves to mentioning this very brief number of these studies is due to the narrowness of the field with a certain number of research pages, and we have limited ourselves to mentioning what is recent from them, and that there are many sources It can be consulted in the literature for those interested in this type of study

Experimental part

Chemicals: **Chemicals:**

The chemicals used during the research were supplied by Switzerland Fluka, British BDH and Spanish PRS companies: sodium hydroxide, hydroxylamine hydrochloride, ethanol, sodium carbonate, sodium nitrite, hydrochloric acid, sulfanilic acid sodium salt, and para-nitro-aniline. While Salicylic acid drug Got from the Nineveh Drug Company (NDI). All compounds were prepared in a standard manner similar to a previous study [17-18].

1- Instruments:

a- UV-Visible Spectrophotometers:

1-A single beam Spectrophotometer instrument manufactured by the British company (Cecil) (Cambridge, England) model (CE 1011/1000) in the range of wavelengths (325-1000nm.).

2-A double beam Spectrophotometer instrument containing a computer made by the Japanese company (Shimadzu), model (UV-1800) produced in 2004 to check the value of (λ_{max}) for the complexes under study and draw the different electronic spectra in the water solvent in the range between (190-1100nm.).

The cells used above were: glass in the visible region and quartz in the invisible region.

b- pH-meter : Made by (JENWAY) Company, Model (3510).

c- **Water bath :** Model (D3165) type (Hanigsen) manufactured by (KOTTERMANN) company.

2- **Preparation of the aqueous drug solution of salicylic acid:** The drug was obtained pure in the form of a white crystalline powder from the Nineveh Drug Company, and it was used directly to prepare its aqueous drug solution at a concentration of (10^{-3}M), to be subsequently reacted with the aqueous solutions of two diazotized reagents (para-nitro aniline) and (sulfanilic acid sodium salt).

3- **Two diazotized reagent solutions:** The two diazotized reagent solutions were prepared at a concentration of ($2x10^{-3}$M) from each of the diazonium salt derived from sulfanilic acid and derived from para-nitro aniline in a standard manner [(3)], and was applied spontaneously each time.

4- **Basic solution of Na_2CO_3:** (0.1M) of Na_2CO_3 Solutions were prepared from sodium carbonate as a base by standard methods [(17-18)], and these solutions were used to control [(16)] the acidic function of the drug complexes at the required values (pH4.9, pH7.1 and pH9.3). Experimentally, different volumes of sodium carbonate solution were added to the two reagent and drug solutions until the required acidity(pH) was obtained, because it was expected that a portion of the carbonate salt (Na_2CO_3) would convert to carbonic acid due to the presence of hydrochloric acid (HCl) with the reagents solution. Thus, a mixture of weak carbonic acid and its salt is created, which acts as a buffer solution to adjust the pH.

5- **Preparation of drug complexes solutions:** The aqueous solutions of the two salicylic acid complexes were prepared under optimal conditions previously obtained, by mixing appropriate quantities of (10^{-3}M) from the diazotized reagent and (0.1M) from the carbonate salt (Na_2CO_3) with (0.2ml) from (10^{-3}M) from the drug solution at a temperature of (25^{o}C) to obtain the required acidic functions : (pH4.9, pH7.1 and pH9.3).

6- **Kinetic study:** The mixture of the solutions mentioned above was fixed each time at the selected temperature (25^{o}C). As the aqueous solutions of the two drug complexes were prepared according to the optimum order of addition, as shown in Table (2). The absorbance of each kinetic complex was followed at its optimum wavelength and until the end of the reaction or reaching its maximum value (λ_{max}). The kinetic equation was applied for the pseudo-first-order reaction, and the rate constant(k), half-life($t_{1/2}$) as well as other activation parameters were calculated.

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Table(1): Numbers, symbols, and names for the two prepared drug complexes.

No. of Complex	Symbol of Complex	Name of Complex Components
1.	SSASS	Salicylic acid drug + Diazotized Sulfanilic Acid Sodium Salt
2.	SPNA	Salicylic Acid Drug + Diazotized para-Nitro Aniline

Table(2): The final optimum conditions for the two prepared drug complexes are under study at a temperature of (25°C) and at (pH4.9, pH7.1 and pH9.3).

Symbol of Complex	Optimum Order of Addition((10^{-3}M)Salicylic acid,Reagent, (0.1M)Na_2CO_3)		Optimum Wavelength (nm.)
SSASS	pH4.9	(0.2ml)Salicylic acid+(2ml)Reagent+(0.05ml)Na_2CO_3.	398
	pH7.1	(0.2ml)Salicylic acid+(2ml)Reagent+(0.15ml)Na_2CO_3.	392
	pH9.3	(0.2ml)Salicylic acid+(2ml)Reagent+(0.25ml)Na_2CO_3.	383
SPNA	pH4.9	(0.2ml)Salicylic acid+(0.15ml)Na_2CO_3+(2ml)Reagent.	405
	pH7.1	(2ml)Reagent+(0.3ml)Na_2CO_3+(0.2ml)Salicylic acid.	404
	pH9.3	(0.6ml)Na_2CO_3+(0.2ml)Salicylic acid+(2ml)Reagent.	393

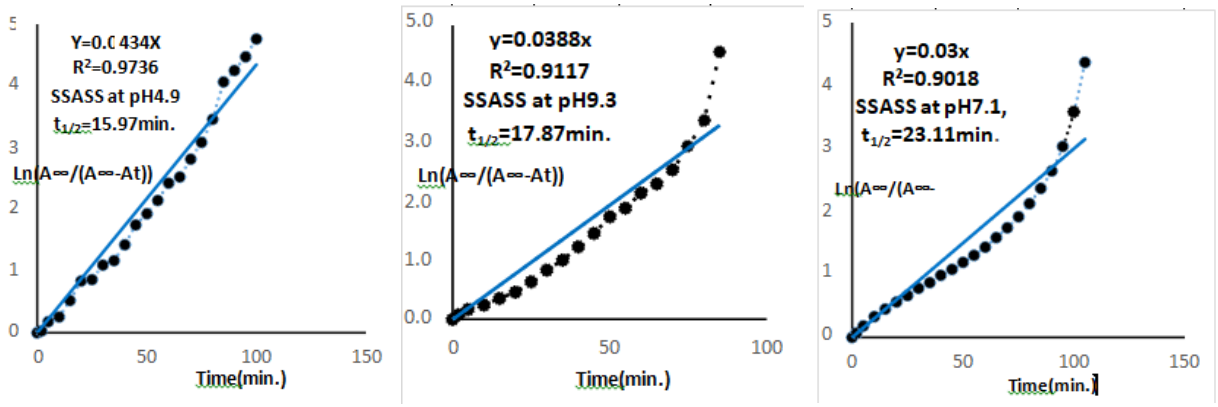
Results and Discussion

The researcher relied on the best optimal conditions for the formation of the two complexes derived from the interaction of the salicylic acid drug once with the diazotized para-nitro aniline reagent and the other with the sulfanilic acid sodium salt reagent that included: the best primitive wavelength, the optimum volume of the reagent, the optimum concentration of the base, the optimum order of addition, Hence, the final optimum wavelength (λ_{max}) of the complex under optimal conditions, as mentioned in our previous study [18-19].In it, we confirmed that the UV and visible spectrum of the two complexes as shown in Table(1) showed spectral bands at the value of (λ_{max}), and as shown in Table(2). These results confirm that there are no spectral interference between the resulting complex and the reactants. Accordingly, this kinetic spectroscopy study was based on the kinematic equation model of the first order in following up the formation of the formed drug complex, by following up the absorption of the resulting complex to a time exceeding (100) minutes. And as shown in Table(3) and Figure(1).

Table(3): Monitoring complex absorbance (SSASS) versus time at a temperature of (25°C), at (pH4.9, pH7.1 and pH9.3), and at the optimum wavelength for each of pH.

Time (min)	Absorbance			$A_\infty-A_t$			$A_\infty/(A_\infty-A_t)$			Ln $\{A_\infty/(A_\infty-A_t)\}$		
	pH4., λ_{max}= 398 nm	pH7.1, λ_{max}= 392 nm	pH9.3, λ_{max}= 383 nm	pH4.9	pH7.1	pH9.3	pH4.9	pH7.1	pH9.3	pH4.9	pH7.1	pH9.3
0	0.000	0.000	0.000	0.350	0.395	0.470	1.00	1.00	1.00	0.000	0.000	0.000
2	0.011	0.027	0.036	0.339	0.368	0.434	1.03	1.07	1.08	0.032	0.071	0.080
5	0.057	0.066	0.072	0.293	0.329	0.398	1.19	1.20	1.18	0.178	0.183	0.166
10	0.079	0.111	0.101	0.271	0.284	0.369	1.29	1.39	1.27	0.256	0.330	0.242
15	0.143	0.144	0.141	0.207	0.251	0.329	1.69	1.57	1.43	0.525	0.453	0.357
20	0.199	0.170	0.173	0.151	0.225	0.297	2.32	1.76	1.58	0.841	0.563	0.459
25	0.202	0.192	0.222	0.148	0.203	0.248	2.36	1.95	1.90	0.861	0.666	0.639
30	0.233	0.214	0.266	0.117	0.181	0.204	2.99	2.18	2.30	1.096	0.780	0.835
35	0.241	0.230	0.298	0.109	0.165	0.172	3.21	2.39	2.73	1.167	0.873	1.005
40	0.266	0.248	0.333	0.084	0.147	0.137	4.17	2.69	3.43	1.427	0.988	1.233
45	0.289	0.261	0.361	0.061	0.134	0.109	5.74	2.95	4.31	1.747	1.081	1.461
50	0.299	0.275	0.388	0.051	0.120	0.082	6.86	3.29	5.73	1.926	1.191	1.746
55	0.309	0.288	0.399	0.041	0.107	0.071	8.54	3.69	6.62	2.144	1.306	1.890
60	0.319	0.301	0.415	0.031	0.094	0.055	11.29	4.20	8.55	2.424	1.436	2.145
65	0.322	0.314	0.423	0.028	0.081	0.047	12.50	4.88	10.00	2.526	1.584	2.303
70	0.329	0.326	0.433	0.021	0.069	0.037	16.67	5.72	12.70	2.813	1.745	2.542
75	0.334	0.337	0.445	0.016	0.058	0.025	21.88	6.81	18.80	3.085	1.918	2.934
80	0.339	0.348	0.454	0.011	0.047	0.016	31.82	8.40	29.38	3.460	2.129	3.380

85	0.344	0.358	0.465	0.006	0.037	0.005	58.33	10.68	94.00	4.066	2.368	4.543
90	0.345	0.367	0.470	0.005	0.028	0.000	70.00	14.11	∞	4.248	2.647	-
95	0.346	0.376	0.466	0.004	0.019	0.004	87.50	20.79	117.5	4.472	3.034	4.766
100	0.347	0.384	0.462	0.003	0.011	0.008	116.7	35.91	58.75	4.759	3.581	4.073
105	0.350	0.390	0.459	0.000	0.005	0.011	∞	79.00	42.73	-	4.369	3.755
110	0.348	0.395	0.444	0.002	0.000	0.026	175.0	∞	18.08	5.165	-	2.895
115	0.344	0.391	0.432	0.006	0.004	0.038	58.33	98.75	12.37	4.066	4.593	2.515
120	0.341	0.382	0.412	0.009	0.013	0.058	38.89	30.38	8.10	3.661	3.414	2.092



Figure(1): Kinetic of complex time at a temperature of (25°C), at at the optimum wavelength for Figure(1) shows that there is a absorbances of the complex (SSASS) that there was a sudden increase in absorbances after (105) minutes complex at (pH4.9), after (110) the drug complex at (pH7.1), and absorbance (SSASS) versus (pH4.9, pH7.1 and pH9.3), and each of pH. direct relationship between the with time. It was also noticed the aforementioned after the formation of the drug minutes after the formation of after (90) minutes after the formation of the drug complex at (pH9.3), and then the absorption to a stable state may be due to the completion of complex formation and the termination of the reaction. And the latter does not affect the values of (λ_{max}) of the complex formed after these times, due to the end of the reaction, and this is confirmed by the values of the half-live times of its reactions, which were: (15.97min. at pH4.9), (23.11min. at pH7.1), (17.87min. at pH9.3) .

In this study, we used the integration method to follow the kinetics of complex formation reactions. When applying the following pseudo first order equation to all the obtained kinetic results:

$Ln\{A_\infty/(A_\infty-A_t)\}= k1.t$----------(1)

And by plotting Ln{$A_\infty/(A_\infty-A_t$)} graph against time (in minutes), we got good straight lines at all pH functions with values (R^2) between (0.9018-0.9736) with slopes equal to the velocity constants (k).) Their interactions, the latter indicates that the drug complex formation reaction is of the first pseudo-first order relative to the drug. From them, the velocity constants of the complex formed at the three acidic functions and at a temperature (25°C) were calculated, which enabled us to calculate the values of its half-lives ($t_{1/2}$), which were calculated from the following second equation: (15.97min. at pH4.9), (23.11 min. at pH7.1), (17.87min. at pH9.3).

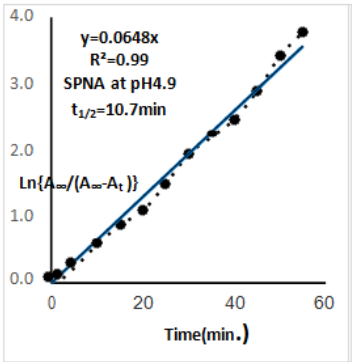
$t_{1/2}=Ln2/k_1$……(2)

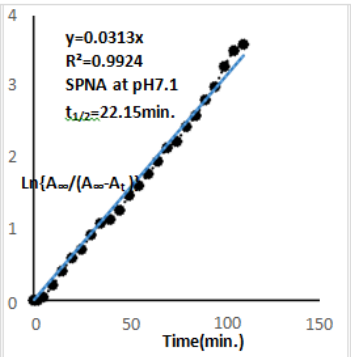
These results were identical to previous studies [6-7] on the kinetics of the reaction of the formation of Azo complexes.

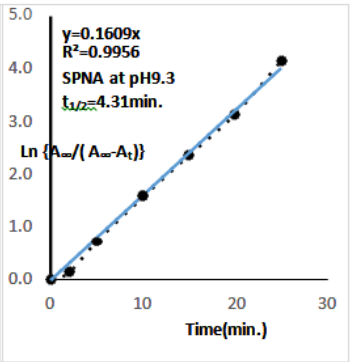
Table(4): Monitoring complex absorbance (SPNA) versus time at a temperature of (25°C), at (pH4.9, pH7.1 and pH9.3), and at the optimum wavelength for each of pH.

Time (min)	Absorbance			$A_\infty-A_t$			$A_\infty/(A_\infty-A_t)$			Ln $\{A_\infty/(A_\infty-A_t)\}$		
	pH4.9, λ_{max}= 405 nm	pH7.1, λ_{max}= 404 nm	pH9.3, λ_{max}= 393 nm	pH = 4.9	pH = 7.1	pH = 9.3	pH = 4.9	pH = 7.1	pH = 9.3	pH = 4.9	pH = 7.1	pH = 9.3
0	0.000	0.000	0.000	0.305	0.401	0.255	1.00	1.00	1.00	0.000	0.000	0.000
2	0.013	0.017	0.034	0.292	0.384	0.221	1.04	1.04	1.15	0.044	0.043	0.143
5	0.060	0.077	0.132	0.245	0.324	0.123	1.24	1.24	2.07	0.219	0.213	0.729
10	0.133	0.135	0.202	0.172	0.266	0.053	1.77	1.51	4.81	0.573	0.410	1.571
15	0.177	0.180	0.231	0.128	0.221	0.024	2.38	1.81	10.63	0.868	0.596	2.363
20	0.202	0.205	0.244	0.103	0.196	0.011	2.96	2.05	23.18	1.086	0.716	3.143
25	0.236	0.241	0.251	0.069	0.160	0.004	4.42	2.51	63.75	1.486	0.919	4.155
30	0.261	0.265	0.255	0.044	0.136	0.000	6.93	2.95	∞	1.936	1.081	-
35	0.271	0.272	0.248	0.034	0.129	0.007	8.97	3.11	36.43	2.194	1.134	3.595
40	0.279	0.288	0.241	0.026	0.113	0.014	11.73	3.55	18.21	2.462	1.267	2.902
45	0.288	0.309	0.239	0.017	0.092	0.016	17.94	4.36	15.94	2.887	1.472	2.769

50	0.295	0.321	0.231	0.010	0.080	0.024	30.50	5.01	10.63	3.418	1.612	2.363
55	0.298	0.333	0.228	0.007	0.068	0.027	43.57	5.90	9.44	3.774	1.774	2.245
60	0.305	0.344	0.222	0.000	0.057	0.033	∞	7.04	7.73	-	1.951	2.045
65	0.297	0.354	0.211	0.008	0.047	0.044	38.13	8.53	5.80	3.641	2.144	1.757
70	0.295	0.358	0.205	0.010	0.043	0.050	30.50	9.33	5.10	3.418	2.233	1.629
75	0.288	0.366	0.201	0.017	0.035	0.054	17.94	11.46	4.72	2.887	2.439	1.552
80	0.284	0.371	0.198	0.021	0.030	0.057	14.52	13.37	4.47	2.676	2.593	1.498
85	0.277	0.377	0.191	0.028	0.024	0.064	10.89	16.71	3.98	2.388	2.816	1.382







90	0.245	0.381	0.188	0.060	0.020	0.067	5.08	20.05	3.81	1.626	2.998	1.337
95	0.244	0.386	0.186	0.061	0.015	0.069	5.00	26.73	3.70	1.609	3.286	1.307
100	0.233	0.389	0.181	0.072	0.012	0.074	4.24	33.42	3.45	1.444	3.509	1.237
105	0.231	0.390	0.177	0.074	0.011	0.078	4.12	36.45	3.27	1.416	3.596	1.185
110	0.222	0.395	0.175	0.083	0.006	0.080	3.67	66.83	3.19	1.301	4.202	1.159
115	0.212	0.401	0.173	0.093	0.000	0.082	3.28	∞	3.11	1.188	-	1.135
120	0.202	0.377	0.151	0.103	0.024	0.104	2.96	16.71	2.45	1.086	2.816	0.897

Figure(2): Kinetic of complex absorbance (SPNA) versus time at a temperature of (25°C), at (pH4.9, pH7.1 and pH9.3), and at the optimum wavelength for each of pH.

Figure (2) shows that there is a direct relationship between the absorbances of the complex (SPNA) with time. It was also noticed that there was a sudden increase in the aforementioned absorbances after (60) minutes after the formation of the drug complex at (pH4.9), after (115) minutes after the formation of the drug complex at (pH7.1), and after (30) minutes after the formation of the drug complex at (pH9.3), and then the absorption to a stable state may be due to the completion of complex formation and the termination of the reaction. And the latter does not affect the values of (λ_{max}) of the complex formed after these times, due to the end of the reaction, and this is confirmed by the values of the half-lives of its reactions, which were: (10.7min. at pH4.9), (22.15min. at pH7.1), (4.31min. at pH9.3) .In this study, we used the integration method to follow the kinetics of complex formation reactions. When applying the following pseudo first order equation (equation(1)) to all the obtained kinetic results And by plotting Ln{$A_\infty/(A_\infty-A_t$)} graph against time (in minutes), we got good straight lines at all pH functions with values (R^2) between (0.9900-0.9956) with slopes equal to the velocity constants (k).) Their interactions, the latter indicates that the drug complex formation reaction is of the first pseudo-first order relative to the drug. From them, the velocity constants of the complex formed at the three acidic functions and at a temperature (25^{o}C) were calculated, which enabled us to calculate the values of its half-live times($t_{1/2}$), which were calculated from equation(2): (10.7min. at pH4.9), (22.15min. at pH7.1), (4.31min. at pH9.3).

These results were identical to previous studies [6-7] on the kinetics of the reaction of the formation of Azo complexes.

From tables (3 and 4), the highest absorbances (A_∞) were obtained for the formation of the two studied complexes at the three pH, their formation expiration times (t_∞), their formation rate constants(k_1), and their half-live times($t_{1/2}$).

It is also noted from Figures (1 and 2) that an increase in the reaction rate constant of the two studied drug complexes at the three pH levels, which inevitably leads to a decrease in their half-live times. And as shown in the following table (5):

Table(5): The values of the highest absorbances (A_∞) for the formation of the two studied complexes at the three pH and λ_{max} levels, their formation expiration times (t_∞), their formation rate constants (k_1), and their half-live times ($t_{1/2}$).

No. of Complex	Symbol of Complex	pH	λ_{max} (nm.)	t_∞ (min.)	A_∞	k_1 (min.$^{-1}$)	($t_{1/2}$) (min.)
1.	SSASS	4.9	398	105	0.350	0.0434	15.97
		7.1	392	110	0.395	0.0300	23.11
		9.3	383	90	0.470	0.0388	17.87
2.	SPNA	4.9	405	60	0.305	0.0648	10.70
		7.1	404	115	0.401	0.0313	22.15
		9.3	393	30	0.255	0.1609	4.31

Table(5) shows the following:

1- The rate constants for the formation of the two complexes under study in the three

acid functions are of the pseudo-first order, and the highest values for the (SSASS) complex were (0.0434 at pH4.9), and the highest values for the (SPNA) complex were (0.1609 at pH9.3). And this discrepancy was consistent with kinetic studies of different interactions in the literature [20-21].

2- The rate constants for the formation of the complexes (k_1) differ according to the reagent due to the different structure of the reagent.

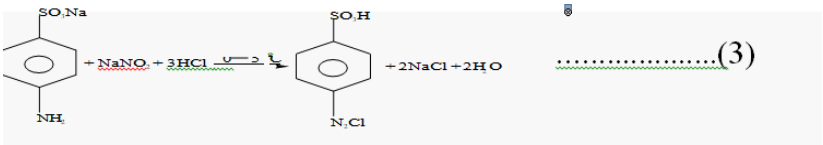
3- The (k_1) of the two complexes differ according to the different values of the acid functions (pH).

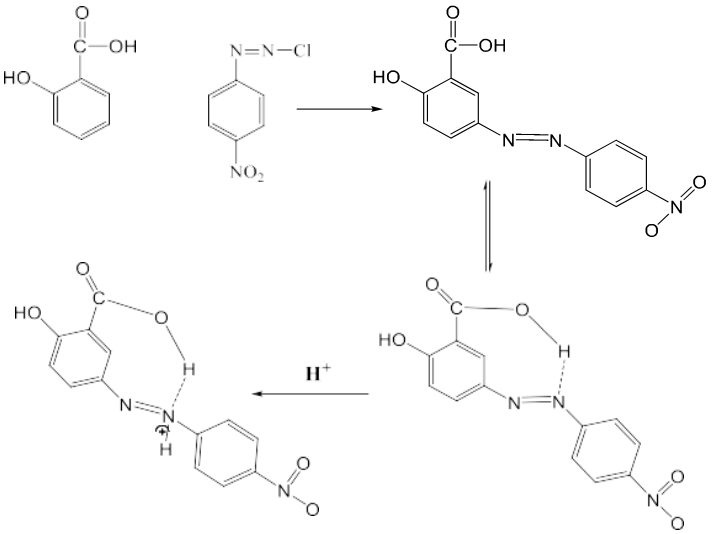
4- The (k_1) of the complexes are exactly inversely proportional to their half-live times($t_{1/2}$).

5- The wavelength of the complex (λ_{max}) changes with the change in the acid function(pH) and the change in the reagent structure forming the complex.

The complex formation reaction (SSASS) takes place according to the following stages[22-24]:

a- Converting the sulfanilic acid sodium salt to the diazotized sulfanilic acid sodium salt according to the following equation:





b- Coupling of the diazotized reagent with the drug under study, as follows:

It is noticed that the azo group is coupled at the (para) site[20-24] relative to the phenolic group, which itself represents the (meta) site relative to the carboxyl group present in the drug.

CONCLUSIONS

1- The values of the formation rate constants of the two complexes (SSASS) and (SPNA) depend on the structure of the reagent forming each of them, as well as their difference according to the different acid functions (pH).

2- The values of the half-live times($t_{1/2}$) of the formation reactions of the two complexes at the three pH levels were exactly the opposite of the rate constant values(k_1) for the formation of the complexes, which are shown in the previous paragraph. This indicates that the faster reaction is completed in less time.

3- The wavelength of the complex (λ_{max}) changes with the change in the acid function (pH) and the change in the reagent structure forming the complex.

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